

# Inventor Search

Ashen 09/623,307

09/02/2004

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L1 306 SEA FILE=HCAPLUS ABB=ON PLU=ON OKU N?/AU  
L2 167 SEA FILE=HCAPLUS ABB=ON PLU=ON NANGO M?/AU  
L3 2173 SEA FILE=HCAPLUS ABB=ON PLU=ON MIYAZAKI H?/AU  
L4 448 SEA FILE=HCAPLUS ABB=ON PLU=ON SAKAKIBARA H?/AU  
L10 3071 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4)  
L11 190 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND TRANSPORT?  
L12 78 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 AND CHARG?  
L13 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 AND NEG?  
L14 7459 SEA FILE=HCAPLUS ABB=ON PLU=ON DRUG DELIVERY SYSTEMS/CT(L) CAR  
R?  
L15 8905 SEA FILE=HCAPLUS ABB=ON PLU=ON DRUG DELIVERY SYSTEMS/CT(L) TRA  
NS?  
L16 12 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND (L14 OR L15)  
L17 14 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 OR L13

=> d l17 ibib abs 1-14

L17 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:70968 HCAPLUS

DOCUMENT NUMBER: 140:309242

TITLE: Possible mechanism of polycation liposome  
(PCL)-mediated gene transfer

AUTHOR(S): Sugiyama, Mayu; Matsuura, Mituso; Takeuchi, Yoshito;  
Kosaka, Jun; **Nango, Mamoru; Oku,**  
**Naoto**

CORPORATE SOURCE: Department of Medical Biochemistry and COE Program in  
the 21st Century, University of Shizuoka School of  
Pharmaceutical Sciences, Yada, Shizuoka, 52-1, Japan  
SOURCE: Biochimica et Biophysica Acta (2004), 1660(1-2), 24-30  
CODEN: BBACAQ; ISSN: 0006-3002

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel gene transfer system utilizing polycation liposomes (PCLs),  
obtained by modifying liposomes with cetyl polyethylenimine (PEI), was  
previously developed. PCLs show notable transfection efficiency with low  
cytotoxicity. However, the mechanism of PCL-mediated gene transfer is  
still unclear. In this study, we examined the intracellular trafficking of  
PCL-DNA complexes by using HT1080 cells, fluorescent probe-labeled  
materials, and confocal laser scan microscopy. We found that the PCL-DNA  
complexes were taken up into cells by the endosomal pathway, since both  
cellular uptake of the complex and gene expression were blocked by  
wortmannin, an inhibitor of this pathway. We also observed that the plasmid  
DNA and cetyl PEI complex became detached from the PCL lipids and was  
preferentially transferred into the nucleus in the form of the complex,  
whereas the PCL lipids remained in the cytoplasmic area, possibly in the  
endosomes. In fact, nigericin, which dissipates the pH gradient across  
the endosomal membrane, inhibited the detachment of lipids from the  
PCL-DNA complex and subsequent gene expression. Taken together, our data  
indicate the following mechanism for gene transfer by PCLs: PCLs  
effectively transfer DNA to endosomes and release cetyl PEI-DNA complexes  
into the cytosol. Furthermore, cetyl PEI also contributes to gene entry  
into the nucleus.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:32570 HCAPLUS  
DOCUMENT NUMBER: 140:99682  
TITLE: Pressure-sensitive adhesives, and transdermal formulations using them  
INVENTOR(S): Miyazaki, Hideo; Ozawa, Hitoshi  
PATENT ASSIGNEE(S): Sumitomo Seika Chemicals Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004010506	A2	20040115	JP 2002-163058	20020604
PRIORITY APPLN. INFO.:			JP 2002-163058	20020604
AB The pressure-sensitive adhesives for transdermal formulations, contain base resins selected from polyethylene, EVA, and amorphous polypropylene, tackifiers, and plasticizers. Flo-Beads (LDPE) 100, Arkon (alicyclic saturated hydrocarbon resin) 50, HV-300 (polybutene) 80, and ascorbic acid (I) 23 g were mixed at 110° and applied on a PET film to give a transdermal formulation showing bond strength (when bonded to a stainless steel) 28 N/cm, good tack (ball number 11), and 95% release of I after 24-h immersion in H2O at 36°.				

L17 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:17825 HCAPLUS  
DOCUMENT NUMBER: 140:65231  
TITLE: Nonirritating adhesives with good drug-releasing properties for transdermal preparations  
INVENTOR(S): Miyazaki, Hideo; Ozawa, Hitoshi  
PATENT ASSIGNEE(S): Sumitomo Seika Chemicals Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004002246	A2	20040108	JP 2002-161180	20020603
PRIORITY APPLN. INFO.:			JP 2002-161180	20020603
AB Title adhesives contain polyethylene, ethylene-vinyl acetate copolymer, and/or amorphous polypropylene as base polymers, tackifiers, plasticizers, and water-absorbing polymers. Thus, a transdermal film containing FLO-BEADS (low-d. polyethylene), Arkon (alicyclic saturated hydrocarbon resin), HV 300 (polybutene), Aqua Calk (modified polyalkylene oxide), and ascorbic acid released 93% ascorbic acid and caused no skin irritation in volunteers.				

L17 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:892648 HCAPLUS  
DOCUMENT NUMBER: 139:369752  
TITLE: Drug- or gene-carrier composition having lowered hemagglutinin activity  
INVENTOR(S): Sakakibara, Hiroyuki; Hara, Hiroto; Ueda, Yasuji; Hasegawa, Mamoru; You, Jun

PATENT ASSIGNEE(S): Dnavec Research Inc., Japan  
 SOURCE: PCT Int. Appl., 80 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003092738	A1	20031113	WO 2003-JP5527	20030430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: JP 2002-129026 A 20020430

AB It is intended to provide a drug- or gene-carrier composition having a lowered hemagglutinin activity. A drug- or gene-carrier composition having a lowered hemagglutinin activity (compared to the case without the addition) can be successfully constructed by adding a compound to an envelope protein having a hemagglutinin activity of a minus strand RNA virus. For example, a virus vector provided in an embodiment shows significantly lowered erythrocyte agglutination activity and hemolytic activity and thus the stability of the vector in blood is remarkably elevated. The drug- or gene-carrier composition thus provided can be adequately used in transferring a drug or a gene into a living body. A NLS-LacZ gene-encoding Sendai virus vector (SeV) was reacted with polyethylene glycol succinimidyl propionic acid derivative, and tested for its hemolysis activity in rat and gene transformation in HeLa cell.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:423404 HCAPLUS

DOCUMENT NUMBER: 139:154707

TITLE: Polycation liposome-mediated gene transfer in vivo

AUTHOR(S): Matsuura, Mitsuo; Yamazaki, Yukako; Sugiyama, Mayu;  
 Kondo, Masami; Ori, Hidetsugu; **Nango, Mamoru**  
 ; **Oku, Naoto**

CORPORATE SOURCE: Department of Medical Biochemistry and COE Program in the 21st Century, University of Shizuoka School of Pharmaceutical Sciences, Yada, Shizuoka, Japan

SOURCE: Biochimica et Biophysica Acta (2003), 1612(2), 136-143  
 CODEN: BBACAQ; ISSN: 0006-3002

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The polycation liposome (PCL), a recently developed gene transfer system, is simply prepared by a modification of liposomes with cetylated polyethylenimine (PEI), and shows remarkable transgene efficiency with low cytotoxicity. In the present study, we investigated the applicability of PCLs for in vivo gene transfer, since the PCL-mediated transgene

efficiency was found to be maintained in the presence of serum. PCLs composed of dioleoylphosphatidylethanolamine (DOPE) with 5 mol% cetyl PEI (PEI average mr. weight 1800), were superior for transfection to those of dipalmitoylphosphatidylcholine (DPPC) and cholesterol (2:1 as molar ratio) with 5 mol% cetyl PEI in vitro, although the latter PCLs were more efficient for gene transfer in vivo. PCL-DNA complexes were injected into mice via a tail or the portal vein, with the DNA being a plasmid encoding green fluorescent protein (GFP) or luciferase; and the expression was monitored qual. or quant., resp. Tail vein injection resulted in high expression of both GFP and luciferase genes in lung, and portal vein injection resulted in high expression of both genes in the liver. Concerning the gene delivery efficiency, the PCL was found to be superior to PEI or cetyl PCL alone. The optimal conditions for in vivo transfection with PCLs were also examined

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:856668 HCAPLUS

DOCUMENT NUMBER: 137:145256

TITLE: A novel non-viral gene transfer system, polycation liposomes

AUTHOR(S): Oku, Naoto; Yamazaki, Yukako; Matsuura, Mitsuo; Sugiyama, Mayu; Hasegawa, Mamoru; Nango, Mamoru

CORPORATE SOURCE: School of Pharmaceutical Sciences, Department of Medical Biochemistry, University of Shizuoka, Yada, Shizuoka, 422-8526, Japan

SOURCE: Advanced Drug Delivery Reviews (2001), 52(3), 209-218  
CODEN: ADDREP; ISSN: 0169-409X

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. To develop a novel non-viral gene transfer system, liposome was modified with cetylated polyethylenimine (PEI). This polycation liposome (PCL) showed remarkable transfection efficiency to COS-1 cells in vitro, in comparison with conventional cationic liposome preps. Cytotoxicity against COS-1 cells and hemolytic activity of PCL or PCL-DNA complex were quite low in comparison with conventional cationic liposomes. Most conventional cationic liposomes require phosphatidylethanolamine or cholesterol as a component, though PCL did not. Egg yolk phosphatidylcholine- and dipalmitoylphosphatidylcholine-based PCL were as effective as dioleoylphosphatidylethanolamine-based PCL for gene transfer. Furthermore, the transfection efficacy of PCL was enhanced, instead of being diminished, in the presence of serum. Effective gene transfer was observed in all eight malignant and two normal line cells tested as well as in COS-1 cells. The effect of the mol. weight of PEI on PCL-mediated gene transfer was examined, and observed that PEIs with a mol. weight of 600 and

1800

Da were quite effective but PEI of 25000 was far less effective. Effectiveness of gene transfer by using PCL was also observed in vivo: GFP and Luciferase genes were effectively expressed in mouse. We also discussed the mechanism of gene transfer by PCL. Taken together, PCL represents a new system useful for transfection and gene therapy.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:476549 HCAPLUS

DOCUMENT NUMBER: 133:182871  
 TITLE: Polycation liposomes, a novel nonviral gene transfer system, constructed from cetylated polyethylenimine  
 AUTHOR(S): Yamazaki, Y.; **Nango, M.**; Matsuura, M.; Hasegawa, Y.; Hasegawa, M.; **Oku, N.**  
 CORPORATE SOURCE: Department of Radiobiochemistry, School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, 422-8526, Japan  
 SOURCE: Gene Therapy (2000), 7(13), 1148-1155  
 CODEN: GETHEC; ISSN: 0969-7128  
 PUBLISHER: Nature Publishing Group  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A novel gene transfer system was developed by using liposomes modified with cetylated polyethylenimine (PEI, MW 600). This polycation liposome, PCL, showed remarkable transfection efficiency as monitored by the expression of the GFP reporter gene. Most conventional cationic liposomes require phosphatidylethanolamine or cholesterol as a component, although PCLs did not. Egg yolk phosphatidylcholine- and dipalmitoylphosphatidylcholine-based PCL were as effective as dioleoylphosphatidylethanolamine-based PCLs for gene transfer. Concerning the cytotoxicity against COS-1 cells and hemolytic activity, the PCL was superior to conventional cationic liposome prepns. Furthermore, the transfection efficacy of PCLs was enhanced, instead of being diminished, in the presence of serum. Effective gene transfer was observed in all eight malignant and two normal cells line tested, as well as in COS-1 cells. We also examined the effect of the mol. weight of PEI on PCL-mediated gene transfer, and observed that PEI with a MW of 1800 Da was as effective as that with one of 600, but that PEI of 25 000 was far less effective. Finally, an in vivo study was done in which GFP was effectively expressed in mouse liver after injection of PCL via the portal vein. Thus, PCL represents a new system useful for transfection and gene therapy.  
 REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:566120 HCAPLUS  
 DOCUMENT NUMBER: 131:189730  
 TITLE: Compositions for **transporting negatively charged** substances  
 INVENTOR(S): **Oku, Naoto; Nango, Mamoru; Miyazaki, Hideki; Sakakibara, Hiroyuki**  
 PATENT ASSIGNEE(S): Dnavec Research Inc., Japan  
 SOURCE: PCT Int. Appl., 79 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943752	A1	19990902	WO 1999-JP954	19990226
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2321200	AA	19990902	CA 1999-2321200	19990226
PRIORITY APPLN. INFO.:			JP 1998-48187	A 19980227
			WO 1999-JP954	W 19990226

AB Novel **transport** carriers comprising polyalkylimines having two or more hydrophobic groups transferred thereinto. It is found out that use of these carriers makes it possible to transfer genes into cells at a high transfer efficiency. Polyethyleneimine was treated with cetyl bromide. Liposomes were formed with the obtained alkylated polyethyleneimine and dioleoylphosphatidylethanolamine. Green fluorescent protein-coded plasmid pEGFP-C1 was incubated with a solution of the liposomes. The liposome/plasmid complex was added to a culture of COS-1 cell and an enhanced gene expression was observed

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:29512 HCAPLUS

DOCUMENT NUMBER: 130:242222

TITLE: Application of Surface-Coated Liposomes for Oral Delivery of Peptide: Effects of Coating the Liposome's Surface on the GI Transit of Insulin

AUTHOR(S): Iwanaga, Kazunori; Ono, Satoshi; Narioka, Kohji; Kakemi, Masawo; Morimoto, Kazuhiro; Yamashita, Shinji; Namba, Yukihiro; **Oku, Naoto**

CORPORATE SOURCE: Department of Pharmaceuticals, Osaka University of Pharmaceutical Sciences, Takatsuki Osaka, 569-1094, Japan

SOURCE: Journal of Pharmaceutical Sciences (1999), 88(2), 248-252

CODEN: JPMSAE; ISSN: 0022-3549

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We prepared two kinds of surface-coated liposomes and investigated their potencies as oral dosage forms for peptide drugs by focusing on their effects on the gastrointestinal (GI) transit of drugs. The surface of the liposomes was coated with poly(ethylene glycol) 2000 (PEG-Lip) or the sugar chain of mucin (Mucin-Lip). As a model peptide drug, insulin was encapsulated in these liposomes. Coating the surface with poly(ethylene glycol) was found to reduce the transit rate of liposomes in the small intestine after oral administration to rats in vivo. Mucin-Lip was retained in the stomach longer than PEG-Lip or uncoated liposomes. The effect of surface coating on the intestinal transit of liposomes was determined by means of in situ single pass perfusion in the rat small intestine. Statistical moment anal. was applied to the outflow pattern of both liposomes and encapsulated insulin. The mean transit time (MTT) and deviation of transit time (DTT) in the intestinal tract were calculated. The MTT of PEG-Lip was much longer than those of uncoated liposomes and Mucin-Lip and was significantly shortened after removal of the intestinal mucous layer. These results indicated that PEG-Lip interacts strongly with the intestinal mucous layer, leading to its slow transit in the intestine. In contrast, coating the liposome's surface with mucin did not affect either the MTT or DTT of liposomes in the intestine. This result is in accordance with the in vivo observation that Mucin-Lip was highly retained in the stomach, but not in any region of the small intestine in vivo. Both the MTT and DTT values of insulin encapsulated in PEG-Lip and Mucin-Lip were almost the same as those of liposomes themselves, suggesting that surface-coated liposomes retained insulin in the intestinal tract. However, MTT and DTT of insulin were significantly shorter than those of uncoated liposomes because these liposomes degraded and released significant amts. of insulin during single pass perfusion. The ability of surface-coated liposomes, especially of PEG-Lip, to interact

with

the mucus layer and slow the transit rate in the GI tract is considered desirable for oral delivery of peptide drugs. Modification of the liposomal surface with appropriate materials, therefore, should be an effective method by which to achieve the oral delivery of peptide drugs.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:400316 HCAPLUS

DOCUMENT NUMBER: 129:99916

TITLE: Enhanced in vitro percutaneous penetration of salicylate by ion pair formation with alkylamines

AUTHOR(S): Kadono, Masanori; Kubo, Kazuyoshi; **Miyazaki, Hirohisa**; Tojyo, Nobuteru; Nakagawa, Shinsaku; Miyashita, Kazuyuki; Imanishi, Takeshi; Rytting, J. Howard; Mayumi, Tadanori

CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Osaka University, Osaka, 565-0871, Japan

SOURCE: Biological & Pharmaceutical Bulletin (1998), 21(6), 599-603

CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The apparent octanol/water partition coefficient (APC) of salicylate (SA) increased as the concentration of alkylamine (amyl, hexyl, heptyl, octyl and nonylamine) in aqueous phase increased, presumably through intermol. ion pair formation between the **neg. charged** SA moiety and the alkylamine cation. The true partition coefficient (TPC) and the formation constant (Kf) of the ion pair were calculated from the partition data. The skin permeability of SA increased as the APC of SA increased, when 20-fold molar excess of alkylamine was added to the donor compartment. Permeability of ion pairs (PAB) from the aqueous phase to a shed snake skin was estimated from the permeability data assuming 1:1 ion pair. The methylene group contribution to the free energy of transfer of ion pairs from water to the shed snake skin was less than the reported value for nonionized drugs. This suggests that the ion pair is more polar by nature than nonionized mols., even if ionic characteristics are masked to some extent by ion pair formation.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:394996 HCAPLUS

DOCUMENT NUMBER: 129:117402

TITLE: A new interpretation of salicylic acid transport across the lipid bilayer: implications of pH-dependent but not carrier-mediated absorption from the gastrointestinal tract

AUTHOR(S): Takagi, Masanori; Taki, Yoko; Sakane, Toshiyasu; Nadai, Tanekazu; Sezaki, Hitoshi; **Oku, Naoto**; Yamashita, Shinji

CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Setsunan University, Hirakata, 573-01, Japan

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1998), 285(3), 1175-1180

CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Transport of several monocarboxylic acids across the lipid bilayer was examined in liposomes consisting of egg yolk phosphatidylcholine and cholesterol. In the presence of inward proton gradient, salicylic acid (SA) was taken up rapidly by liposomes showing overshoot, saturation and competitive inhibition phenomena. These carrier-mediated like profiles of SA uptake can be explained by assuming a very high permeability through the liposomal membrane of protonated SA. Protonated SA in the extraliposomal solution (pH 5.8) was taken up by liposomes rapidly, followed by a redissocn. to anion according to the intraliposomal pH (pH 7.5). The concentration gradient of protonated SA across the liposomal membrane is maintained until the intraliposomal pH decreased to the extraliposomal level, which facilitates the uptake of SA into liposomes. The permeability of the lipid bilayer to several compds. was estimated from the inhibitory effects of those compds. on SA uptake by liposomes. Good linear relationships were observed between their inhibitory effects on the liposomal uptake of SA and the permeability of the intestinal membrane to them determined both in vivo and in vitro. These results clearly indicate that the carrier-independent transport mechanism of monocarboxylic acids observed in liposomes significantly contributes to their absorption from the intestinal tract under physiol. conditions.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:659553 HCAPLUS

DOCUMENT NUMBER: 127:298653

TITLE: Application of liposomes for drug carriers and their topical effect on the skin

AUTHOR(S): Oku, Naoto; Iwanaga, Kazunori; Yamashita, Shinji

CORPORATE SOURCE: Sch. Pharmaceutical Scis., Univ. Shizuoka, Osaka Univ. Pharmaceutical Scis., Shizuoka, 422, Japan

SOURCE: Nippon Keshohin Gijutsusha Kaishi (1997), 31(3), 254-262

CODEN: NKGKF8; ISSN: 0387-5253

PUBLISHER: Nippon Keshohin Gijutsushakai

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB Liposomes have been used as drug carriers in the field of drug delivery systems. Since, liposomes can encapsulate both hydrophilic and hydrophobic materials and are quite safe to use, they could be used as carriers in transdermal therapeutic system, although systematic investigation about the effect of liposomalization of hydrophilic substances on the transdermal adsorption has not been much performed. Therefore, we investigated the effect of liposomalization on hydrophilic materials, and observed that they accumulated relatively high compared with low permeation. This suggests that liposomalization of hydrophilic materials may be useful for topical application rather than TTS. Next, we tried to overcome various problems for use of liposomes as drug carriers after administration into the bloodstream. Since liposomes are the model of biomembrane, they could possess various functions which are observed in biomembranes: many functional liposomes have been developed based on their nature as models of biomembranes. In the present review, we discussed liposomes for site-specific delivering, those for cytosolic delivery of the encapsulated materials, and reticuloendothelial system (RES)-avoiding liposomes for passive targeting to tumor tissues. The actual usefulness of RES-avoiding liposomes for tumor imaging and therapy, as well as for



photodynamic therapy, was demonstrated.

L17 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:447486 HCAPLUS  
DOCUMENT NUMBER: 127:85884  
TITLE: Liposomes  
AUTHOR(S): Oku, Naoto  
CORPORATE SOURCE: Yakugakubu, Shizuoka-kenritsu Daigaku, Shizuoka, 422, Japan  
SOURCE: Igaku no Ayumi (1997), 181(9), 860-861  
CODEN: IGAYAY; ISSN: 0039-2359  
PUBLISHER: Ishiyaku  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB A review with 5 refs., on characterization of liposomes and its application as drug carrier or gene carrier in the drug delivery system and in genetic engineering.

L17 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:4496 HCAPLUS  
DOCUMENT NUMBER: 108:4496  
TITLE: Tumor necrosis factor-induced permeability increase of **negatively charged** phospholipid vesicles  
AUTHOR(S): Oku, Naoto; Araki, Ryuichi; Araki, Hiroko; Shibamoto, Sayumi; Ito, Fumiaki; Nishihara, Tatsuro; Tsujimoto, Masafumi  
CORPORATE SOURCE: Fac. Pharm. Sci., Setsunan Univ., Hirakata, 573-01, Japan  
SOURCE: Journal of Biochemistry (Tokyo, Japan) (1987), 102(5), 1303-10  
CODEN: JOBIAO; ISSN: 0021-924X  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The effect of human tumor necrosis factor (TNF) on the permeability properties of liposomal membranes was investigated. TNF caused an increase in permeability of liposomes containing phosphatidylserine at pH 5-6, as demonstrated by the calcein efflux. However, it did not induce any permeability change in such liposomes at neutral pH. The TNF-induced calcein efflux was also observed when another acidic lipid was used as a component of the liposomes, i.e., phosphatidic acid or dicetyl phosphate. On the other hand, liposomes composed of neutral phospholipids such as phosphatidylcholine, phosphatidylethanolamine, and sphingomyelin showed little increases in permeability when incubated with TNF above pH 5.0. The TNF-induced permeability change was inhibited by the addition of polyaspartic acid, while it was not affected by the presence of 0.5 mM Ca. These data suggest that the **neg. charges** on the liposomal surface trigger the interaction between TNF and liposomes. However, when the pH of the reaction mixture was decreased to 4.5, TNF-induced calcein efflux was observed even from neutral liposomes. When TNF was incubated with 8-anilinonaphthalene-1-sulfonic acid, the fluorescence intensity of this fluorophore increased with a decrease in the pH of the solution from 7 to 5, and a drastic increase in fluorescence was observed at pH 4.5. These data suggest that the hydrophobic region of TNF is also important for liposomal damage. Furthermore, the potencies of TNF and its derivative as to the induction of the permeability change paralleled their cytotoxic effects on mouse L929 cells, suggesting that the effect of TNF on liposomal membranes is related to its biol. action.

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Applicant

Ashen 09/623,307

09/02/2004

L9 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1999:566120 HCAPLUS  
DOCUMENT NUMBER: 131:189730  
ENTRY DATE: Entered STN: 08 Sep 1999  
TITLE: Compositions for transporting negatively charged substances  
INVENTOR(S): Oku, Naoto; Nango, Mamoru; Miyazaki, Hideki; Sakakibara, Hiroyuki  
PATENT ASSIGNEE(S): Dnavec Research Inc., Japan  
SOURCE: PCT Int. Appl., 79 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
INT. PATENT CLASSIF.:  
MAIN: C08L079-02  
SECONDARY: A61K045-00; A61K048-00; A61K047-48; C12N015-00  
CLASSIFICATION: 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

Cmpd. of Cl. 51+52  
not indexed  
in applicant's  
CA Record

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943752	A1	19990902	WO 1999-JP954	19990226
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2321200	AA	19990902	CA 1999-2321200	19990226
PRIORITY APPLN. INFO.:			JP 1998-48187	A 19980227
			WO 1999-JP954	W 19990226

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9943752	ICM	C08L079-02
	ICS	A61K045-00; A61K048-00; A61K047-48; C12N015-00

ABSTRACT:

Novel transport carriers comprising polyalkylimines having two or more hydrophobic groups transferred thereinto. It is found out that use of these carriers makes it possible to transfer genes into cells at a high transfer efficiency. Polyethyleneimine was treated with cetyl bromide. Liposomes were formed with the obtained alkylated polyethyleneimine and dioleoylphosphatidylethanolamine. Green fluorescent protein-coded plasmid pEGEP-C1 was incubated with a solution of the liposomes. The liposome/plasmid complex was added to a culture of COS-1 cell and an enhanced gene expression was observed

SUPPL. TERM: polyamine prepn drug carrier; gene therapy polyalkylimine prepn  
INDEX TERM: Drug delivery systems  
(carriers; preparation of polyalkylimines as drug carriers)  
INDEX TERM: Plasmids  
(pEGEP-C1; preparation of polyalkylimines as drug carriers)  
INDEX TERM: Amines, biological studies  
ROLE: SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(polyamines, nonpolymeric; preparation of polyalkylimines as drug carriers)  
INDEX TERM: Gene therapy

(preparation of polyalkylimines as drug carriers)  
INDEX TERM: Nucleic acids  
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of polyalkylimines as drug carriers)  
INDEX TERM: 111-83-1, 1-Bromooctane 112-82-3,  
1-Bromohexadecane 143-15-7, 1-Bromododecane  
9002-98-6 40563-82-4 89031-84-5  
99142-42-4  
ROLE: RCT (Reactant); RACT (Reactant or reagent)

(preparation of polyalkylimines as drug carriers)  
INDEX TERM: 113812-13-8P 239119-01-8P  
239119-02-9P 239119-03-0P  
239119-04-1P 239119-05-2P  
239119-06-3P 239119-07-4P  
239119-08-5P 239119-09-6P  
239119-10-9P 239119-11-0P  
239119-12-1P 239119-13-2P  
239119-17-6P 239119-18-7P  
239119-19-8P 239119-20-1P  
239119-21-2P 239119-22-3P  
239119-23-4P 239119-24-5P  
239119-25-6P 239119-26-7P  
239119-27-8P 239119-32-5P  
239119-33-6P 239119-34-7P  
239119-35-8P 239480-83-2P  
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of polyalkylimines as drug carriers)  
INDEX TERM: 112-29-8DP, Decyl bromide, reaction products with  
polyethyleneimine 112-71-0DP, Myristyl bromide,  
reaction products with polyethyleneimine 112-82-3DP  
, Cetyl bromide, reaction products with polyethyleneimine  
112-89-0DP, Stearyl bromide, reaction products with  
polyethyleneimine 143-15-7DP, Lauryl bromide,  
reaction products with polyethyleneimine 9002-98-6DP  
, reaction products with alkyl bromides 239119-14-3P  
239119-15-4P 239119-16-5P  
239119-28-9P 239119-29-0P  
239119-30-3P 239119-31-4P  
239119-36-9P  
ROLE: SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of polyalkylimines as drug carriers)  
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
RECORD.

REFERENCE(S): (1) Institut Neftekhimicheskogo Sintez a Imeni AV Toncheva  
Akademii Nauk SSSR; GB 1459809 A HCAPLUS  
(2) Institut Neftekhimicheskogo Sintez a Imeni AV Toncheva  
Akademii Nauk SSSR; DE 2530042 A HCAPLUS  
(3) Institut Neftekhimicheskogo Sintez a Imeni AV Toncheva  
Akademii Nauk SSSR; US 4032480 A  
(4) Institut Neftekhimicheskogo Sintez a Imeni AV Toncheva  
Akademii Nauk SSSR; JP 52-10400 A 1977  
(5) Khmel'nitsky, Y; Eur J Biochem 1992, V206(3), P737  
MEDLINE  
(6) The Dow Chemical Co; JP 43-8828 B 1968  
(7) Zanta, M; Bioconjugate Chem 1997, V8(6), P839 HCAPLUS

IT 111-83-1, 1-Bromooctane 112-82-3, 1-Bromohexadecane

143-15-7, 1-Bromododecane 9002-98-6 40563-82-4

89031-84-5 99142-42-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of polyalkylimines as drug carriers)

RN 111-83-1 HCAPLUS

CN Octane, 1-bromo- (6CI, 8CI, 9CI) (CA INDEX NAME)

Me- (CH<sub>2</sub>)<sub>7</sub>-Br

RN 112-82-3 HCAPLUS

CN Hexadecane, 1-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Me- (CH<sub>2</sub>)<sub>15</sub>-Br

RN 143-15-7 HCAPLUS

CN Dodecane, 1-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

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RN 9002-98-6 HCAPLUS

CN Aziridine, homopolymer (9CI) (CA INDEX NAME)

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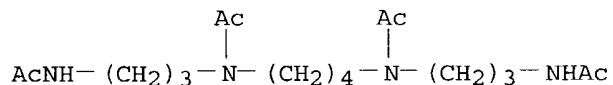
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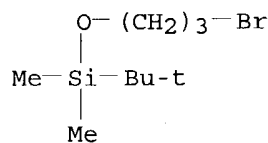
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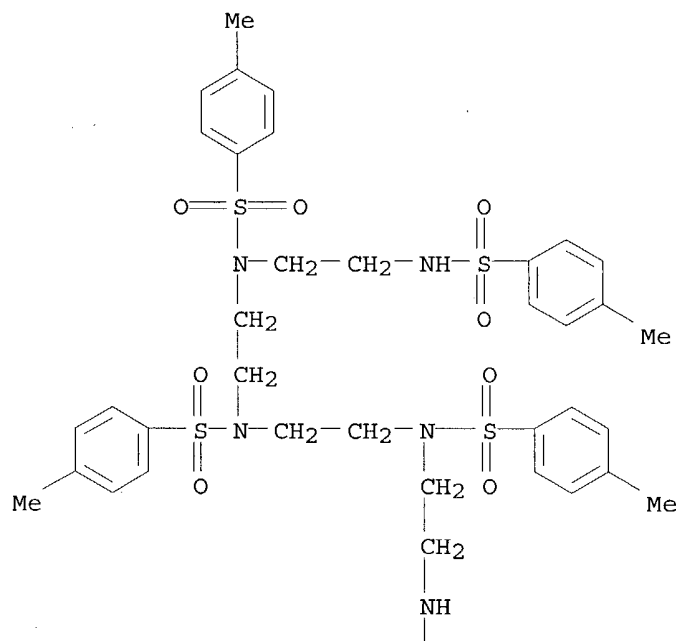
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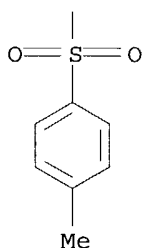


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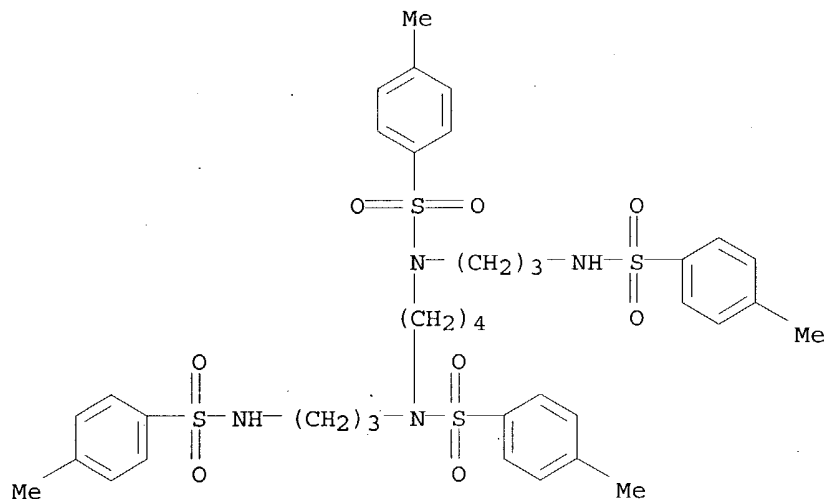
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)

(preparation of polyalkylimines as drug carriers)

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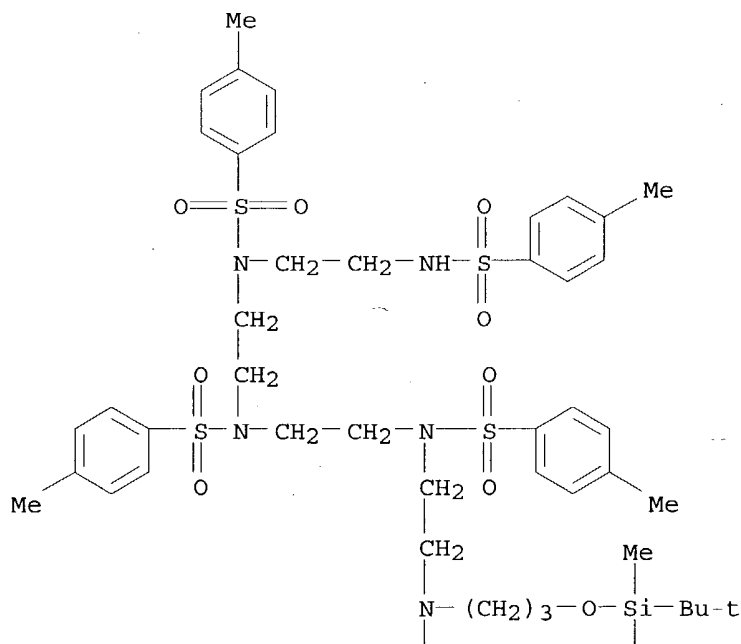
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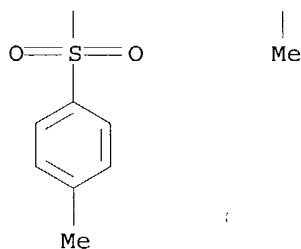
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CN Benzenesulfonamide, 4-methyl-N-[2-[[4-methylphenyl)sulfonyl][2-[[4-methylphenyl)sulfonyl]amino]ethyl]amino]ethyl]-N-[11,11,12,12-tetramethyl-3,6-bis[[4-methylphenyl)sulfonyl]-10-oxa-3,6-diaza-11-silatridec-1-yl]- (9CI) (CA INDEX NAME)

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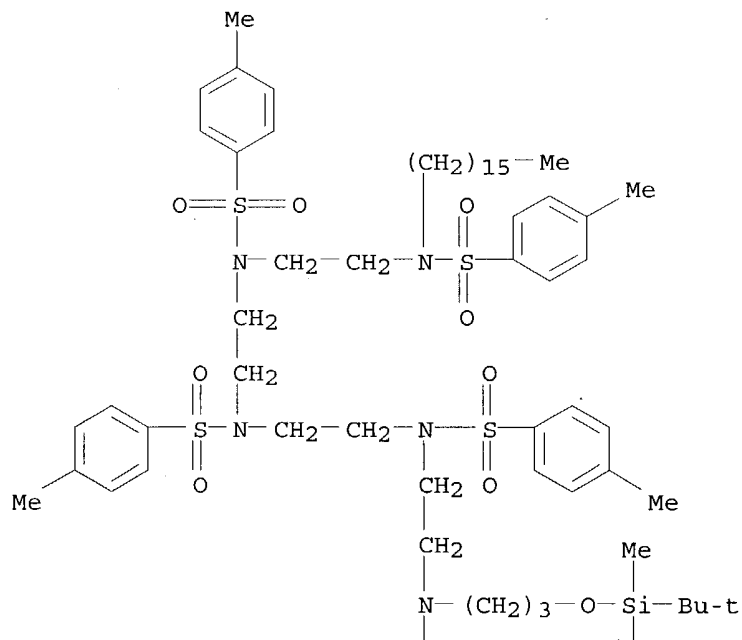


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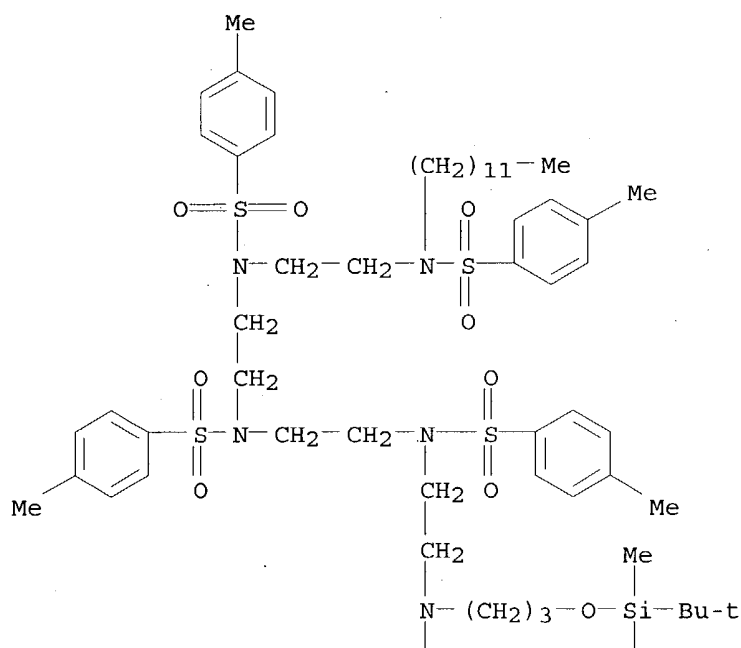
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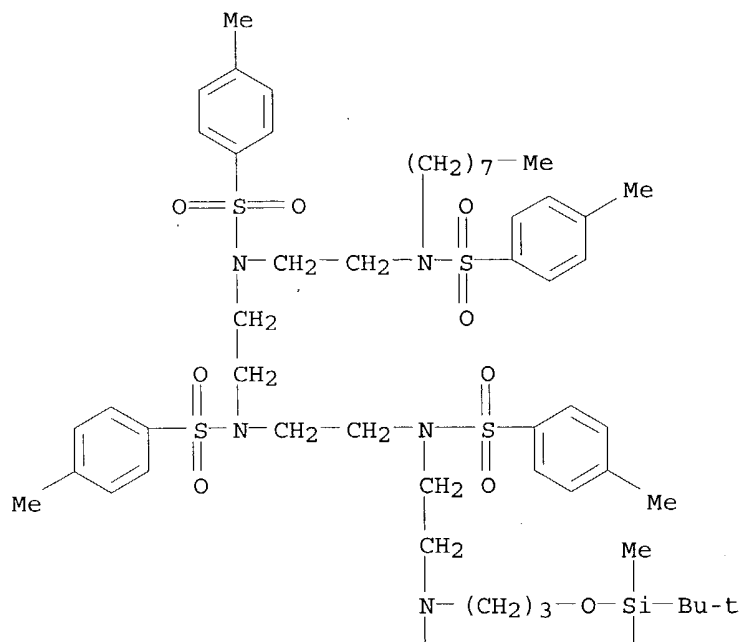
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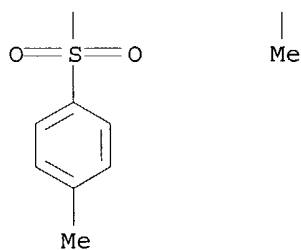
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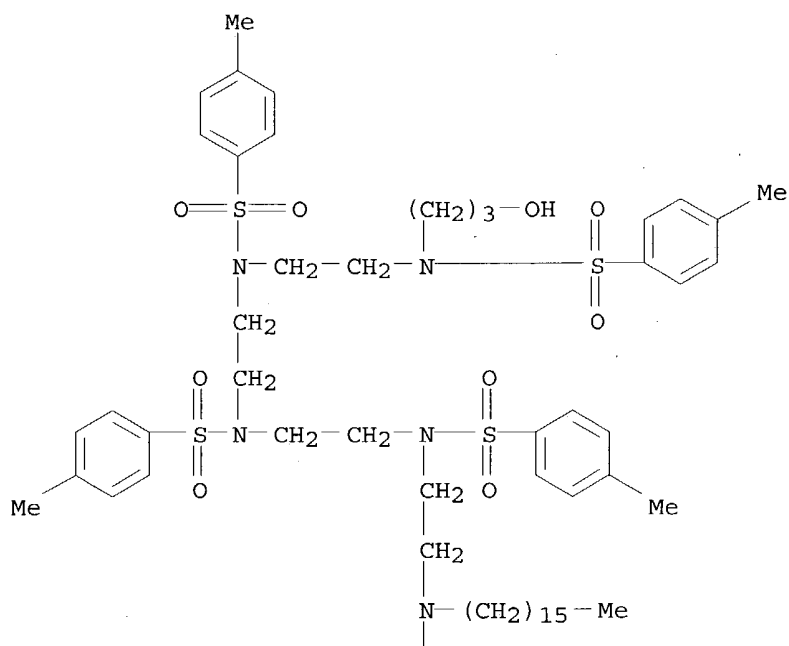


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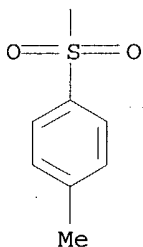


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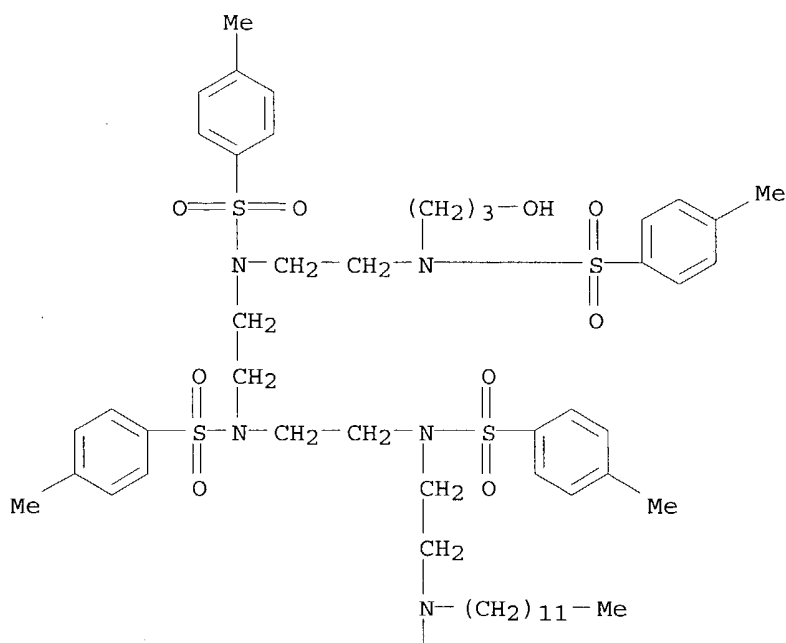


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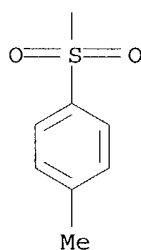


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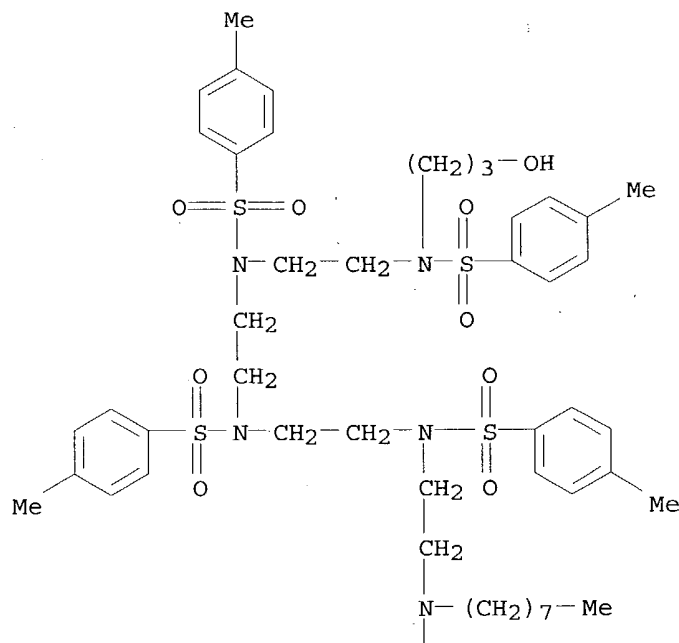


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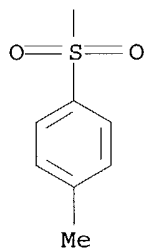


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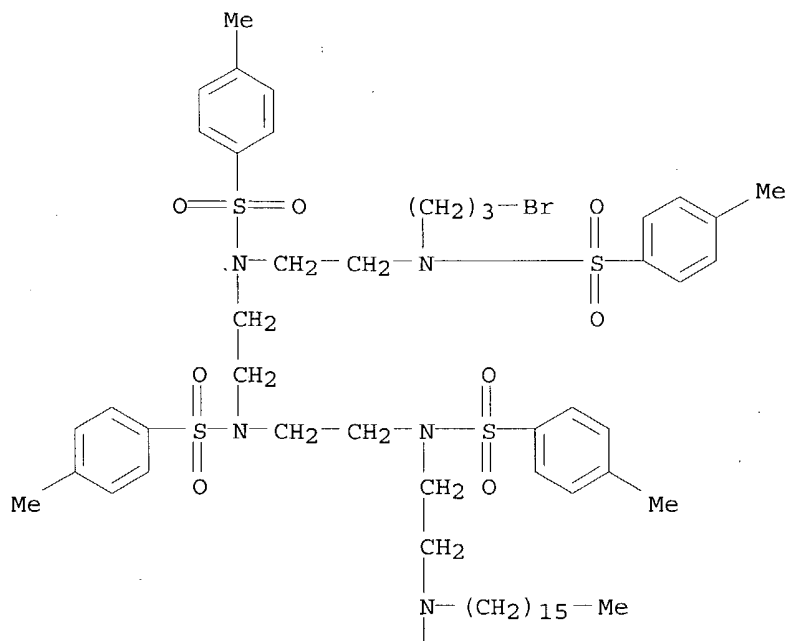


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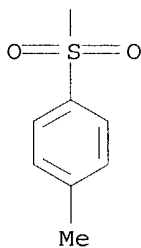


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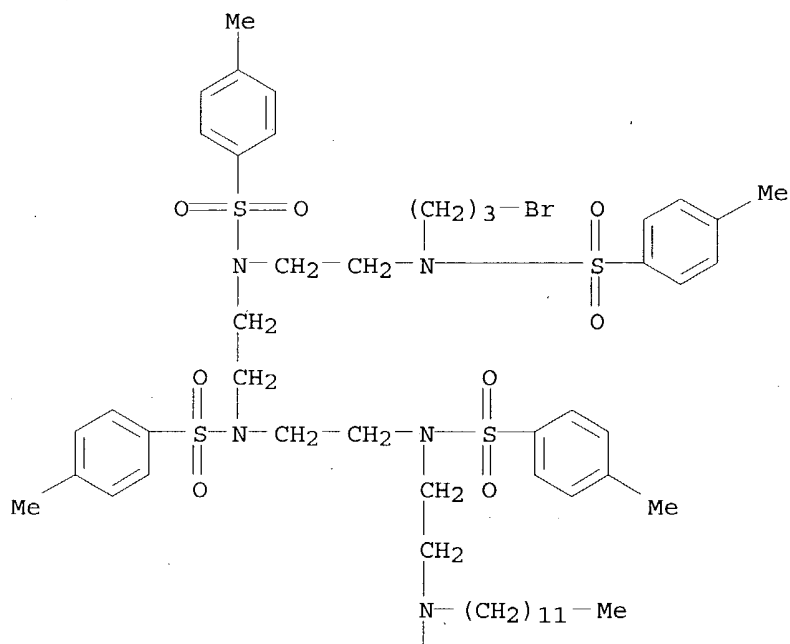


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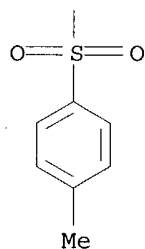


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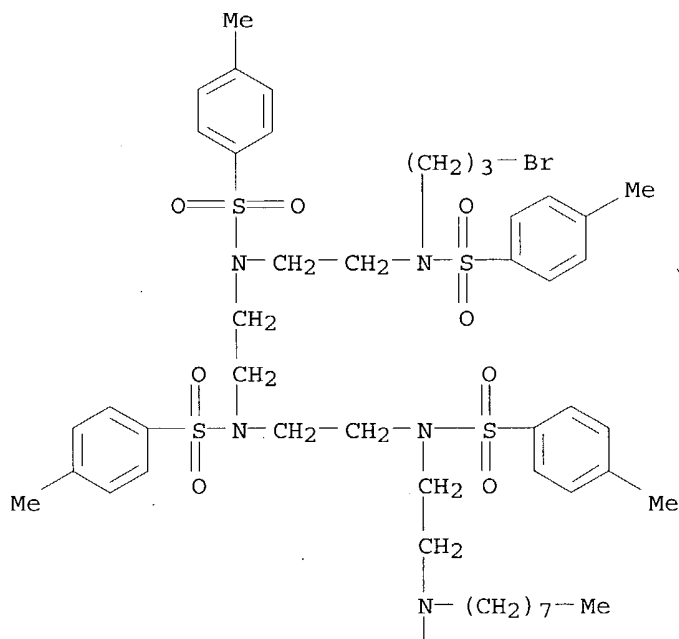


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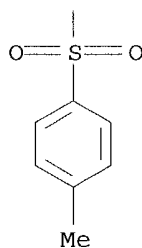


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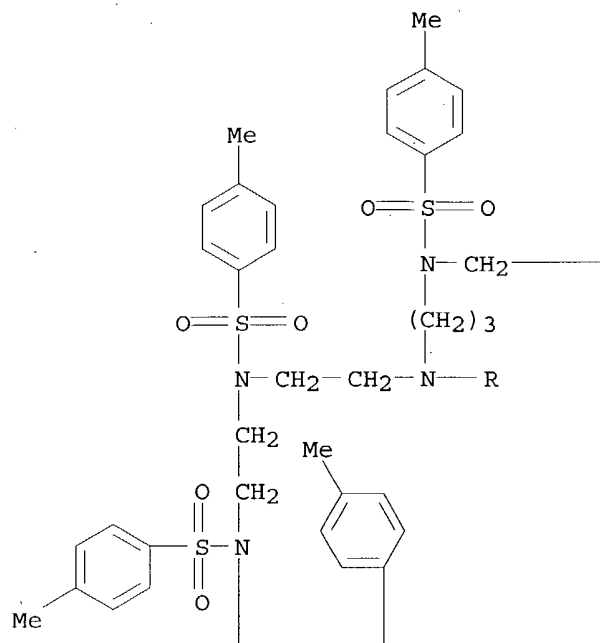
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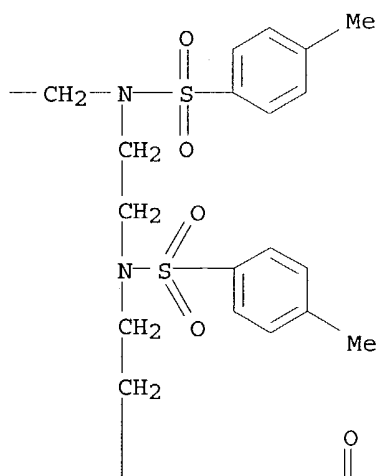
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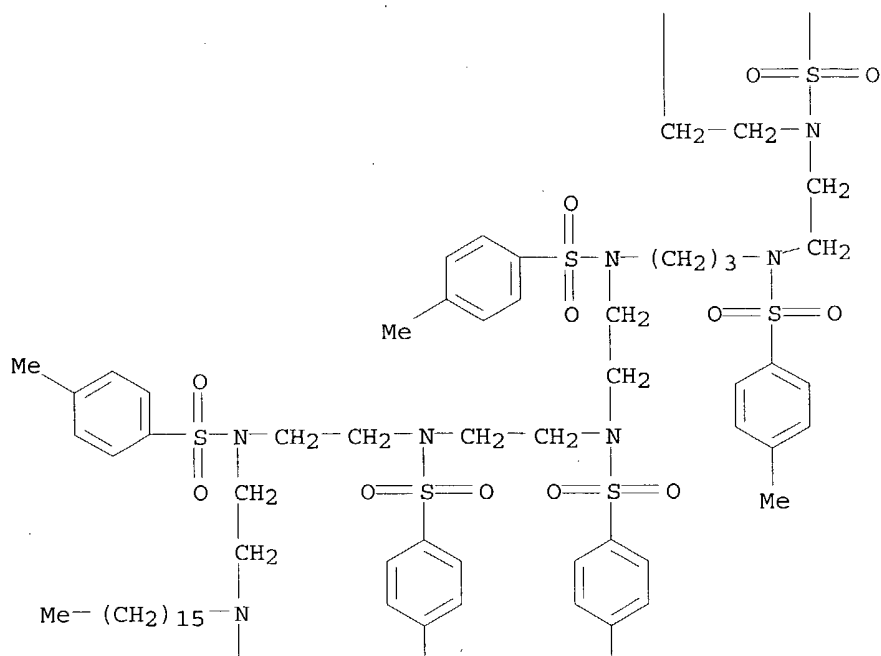
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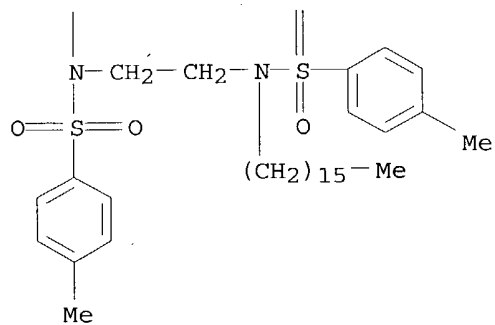
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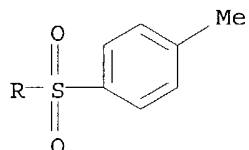
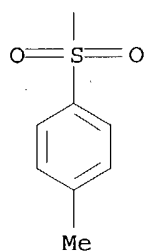
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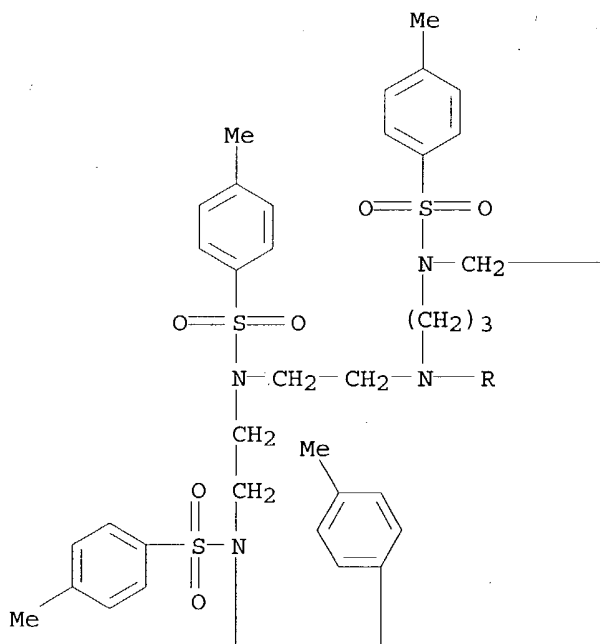


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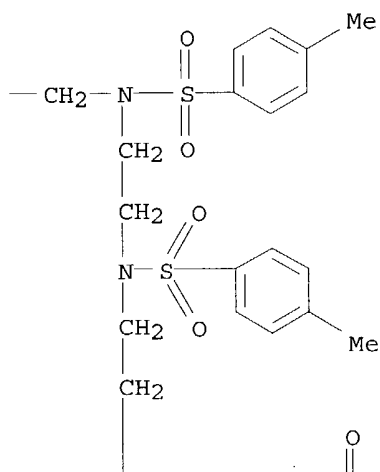


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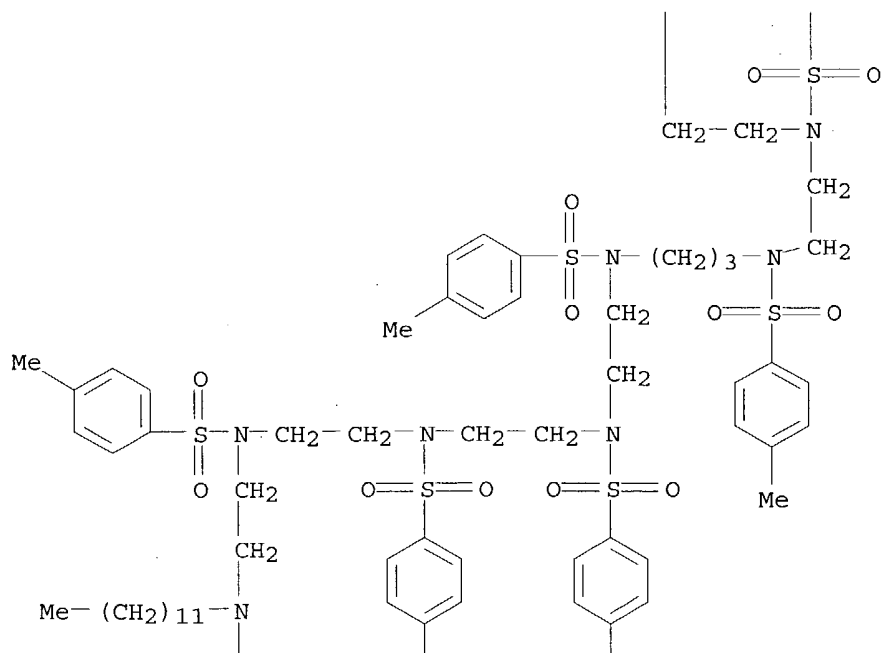
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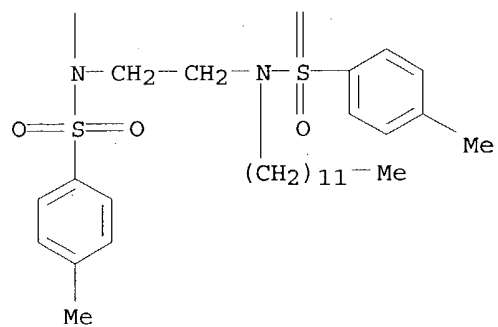
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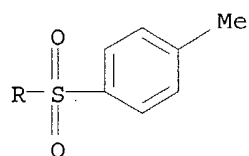
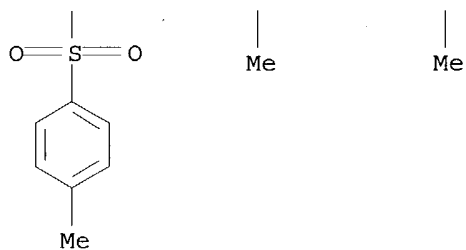
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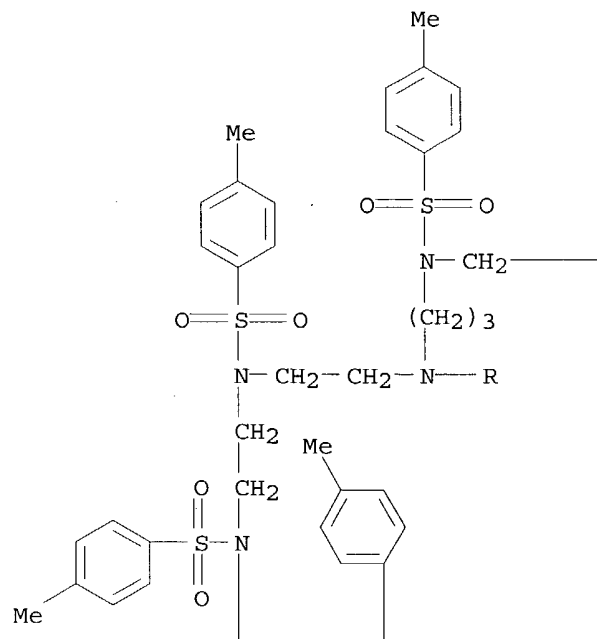


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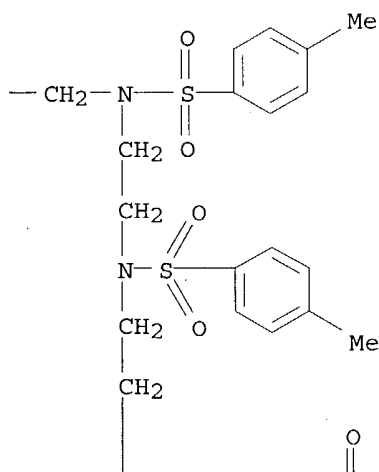


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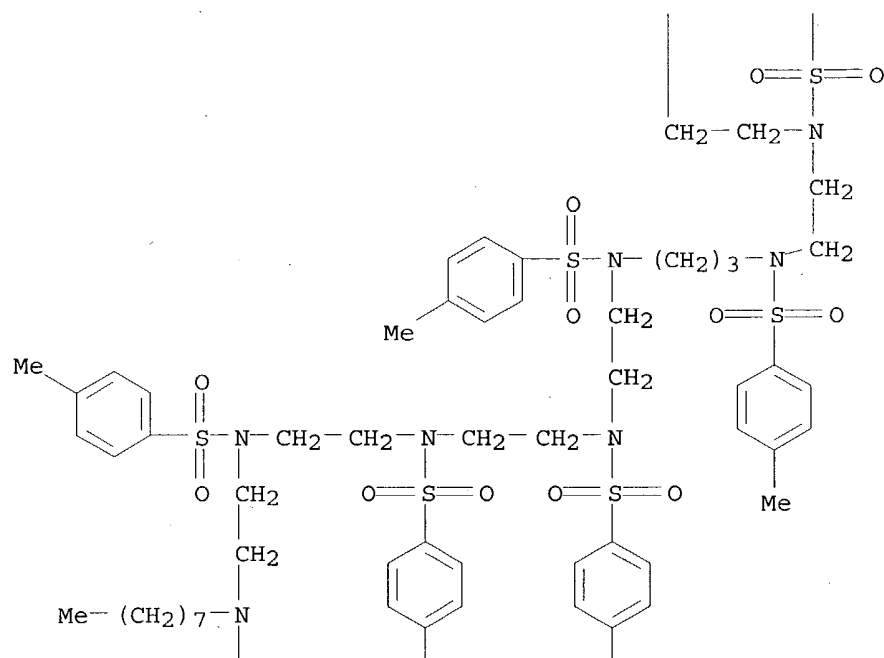
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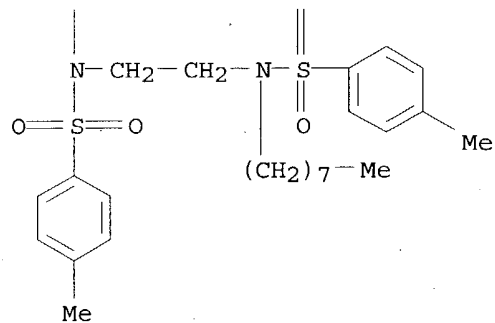
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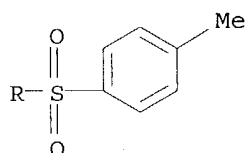
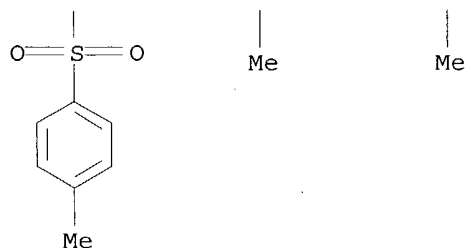
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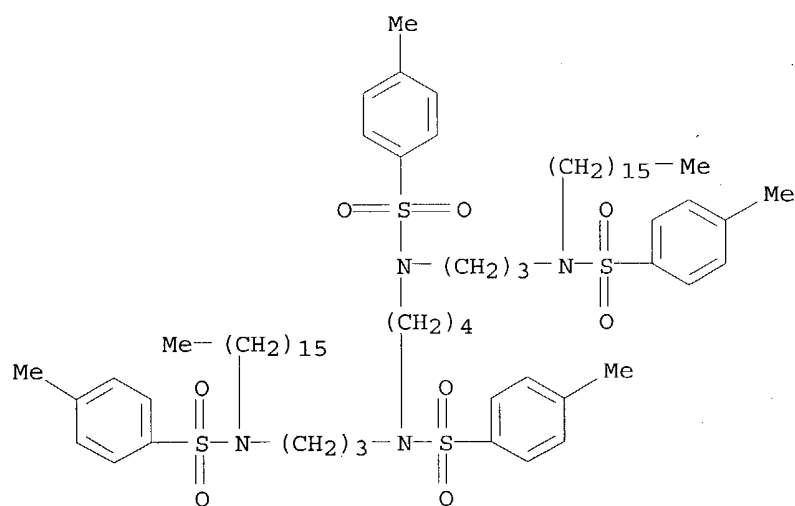


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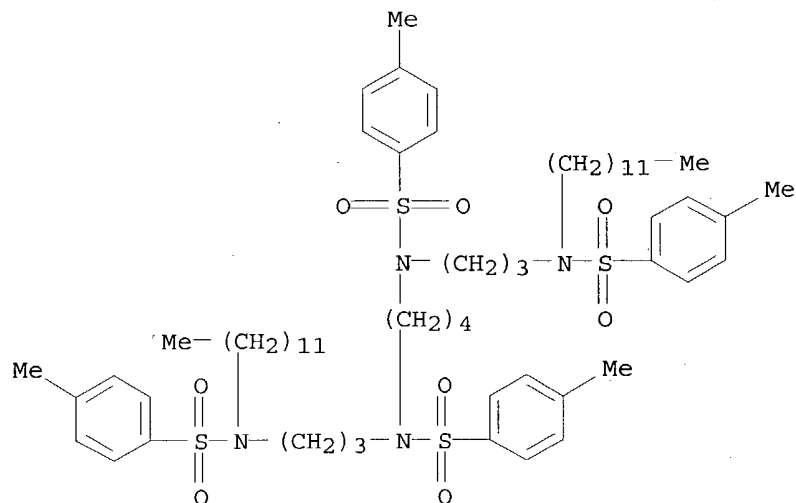
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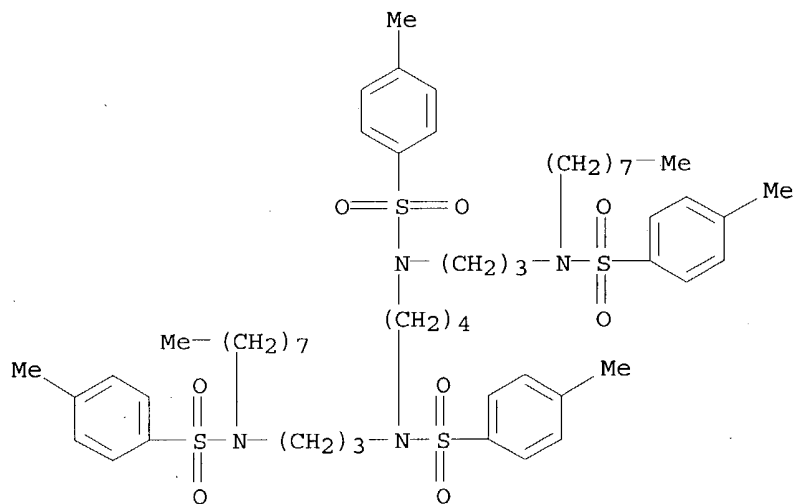
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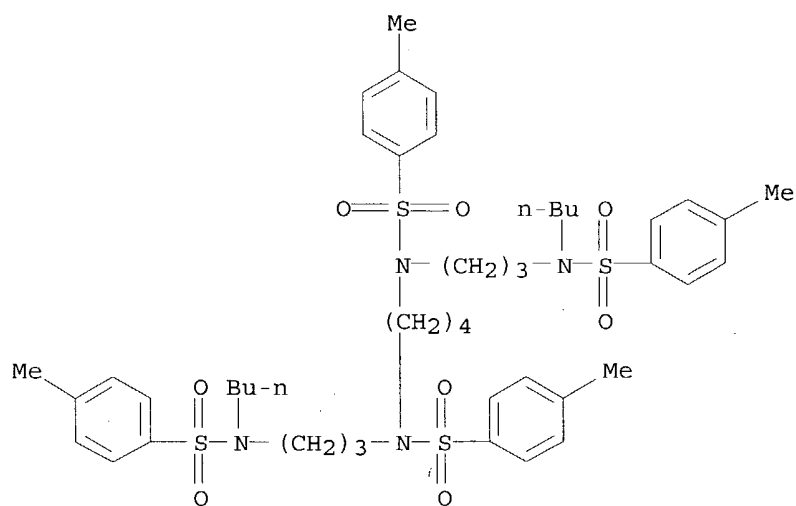
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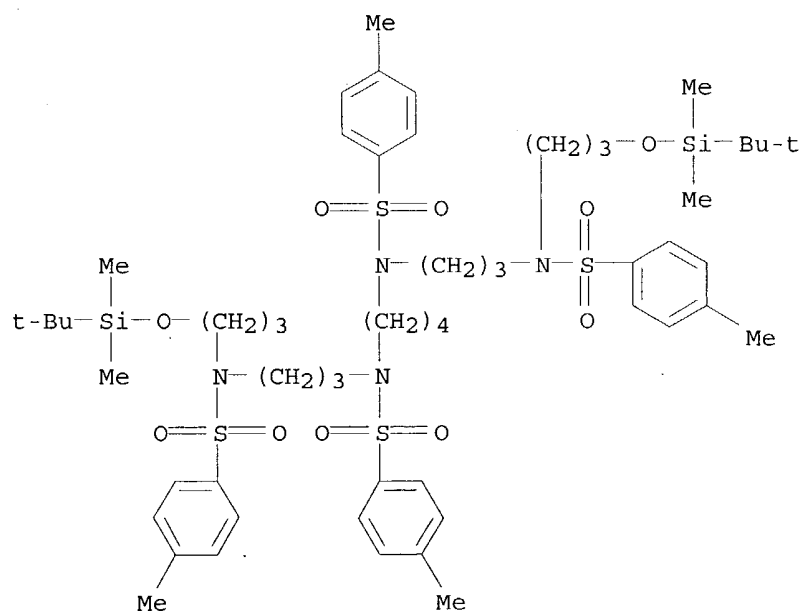
RN 239119-20-1 HCAPLUS

CN Benzenesulfonamide, N,N'-1,4-butanediylbis[N-[[3-[butyl[(4-methylphenyl)sulfonyl]amino]propyl]-4-methyl- (9CI) (CA INDEX NAME)



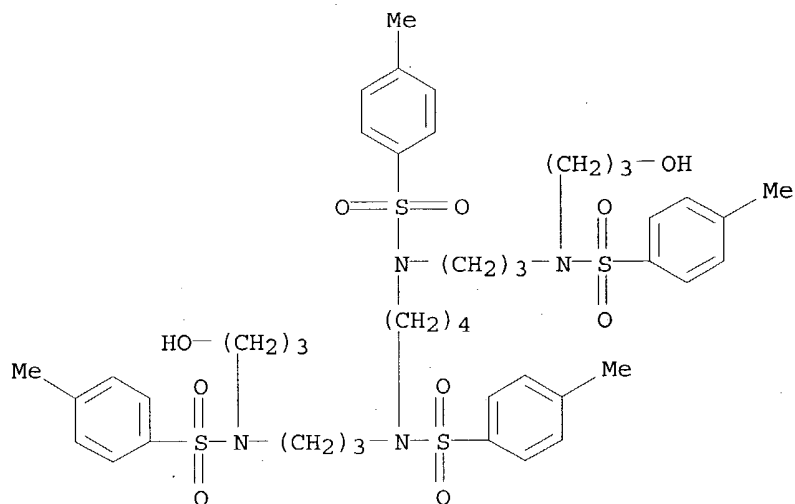
RN 239119-21-2 HCAPLUS

CN Benzenesulfonamide, N,N'-1,4-butanediylbis[N-3-[[3-[[[1,1-dimethylethyl]dimethylsilyl]oxy]propyl][(4-methylphenyl)sulfonyl]amino]propyl]-4-methyl- (9CI) (CA INDEX NAME)



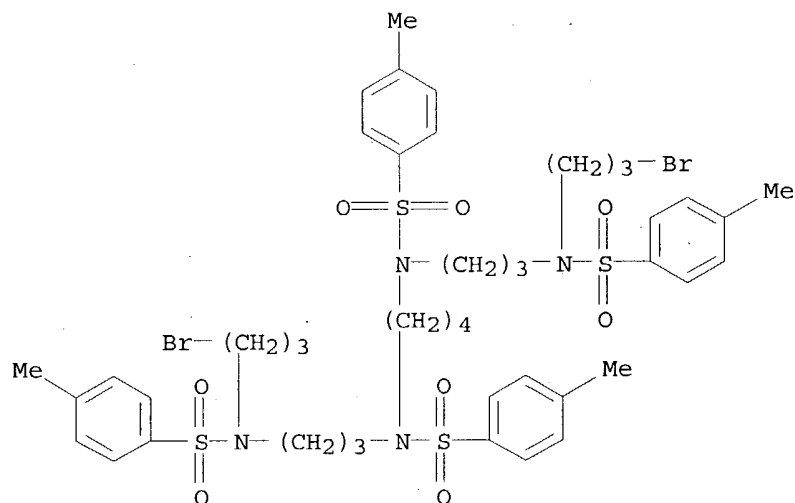
RN 239119-22-3 HCAPLUS

CN Benzenesulfonamide, N,N'-1,4-butanediylbis[N-3-[(3-hydroxypropyl][(4-methylphenyl)sulfonyl]amino]propyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 239119-23-4 HCAPLUS

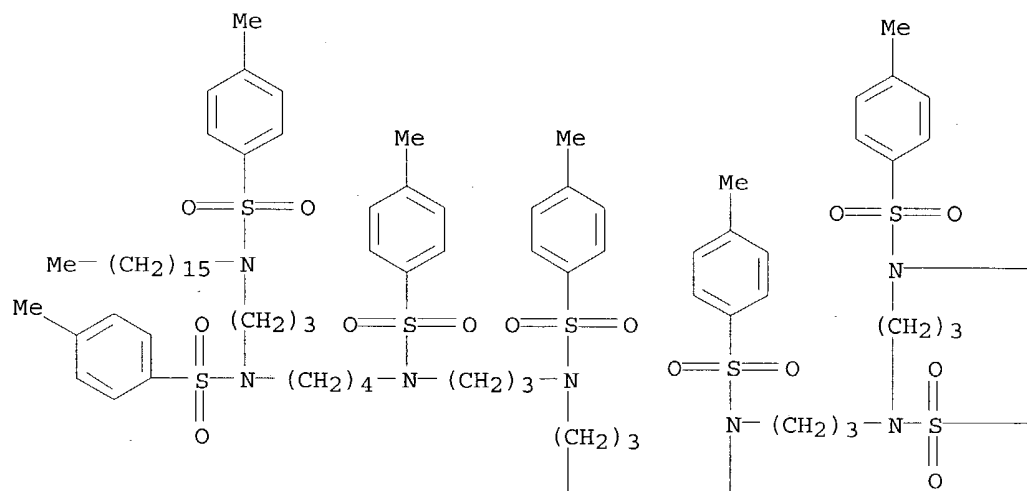
CN Benzenesulfonamide, N,N'-1,4-butanediylbis[N-3-[(3-bromopropyl)](4-methylphenyl)sulfonyl]amino]propyl]-4-methyl- (9CI) (CA INDEX NAME)



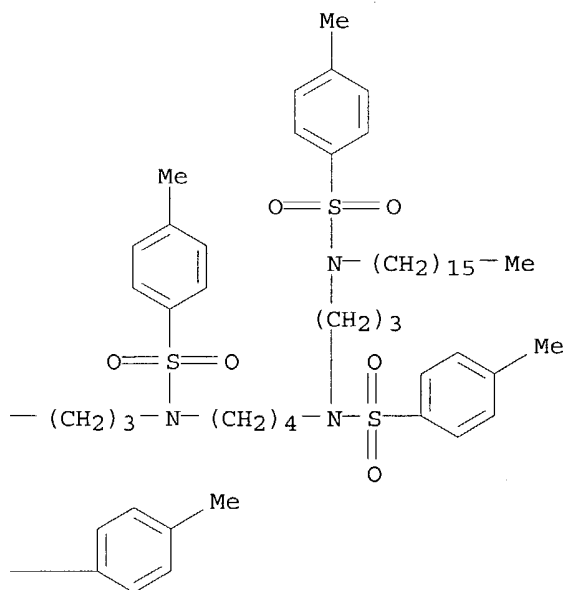
RN 239119-24-5 HCAPLUS

CN Benzenesulfonamide, N,N'-1,4-butanediylbis[4-methyl-N-[4,8,12,17,21-pentakis[(4-methylphenyl)sulfonyl]-4,8,12,17,21-pentaazaheptatriacont-1-yl]- (9CI) (CA INDEX NAME)

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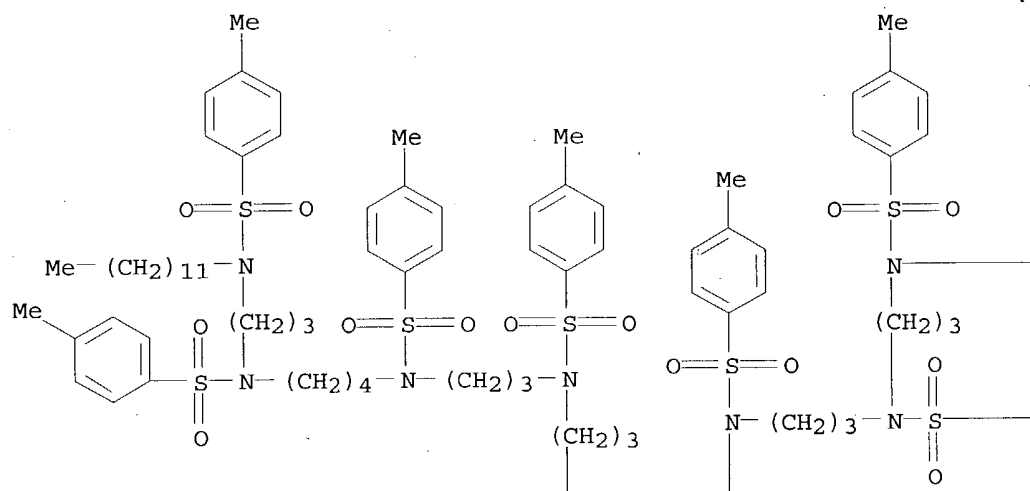


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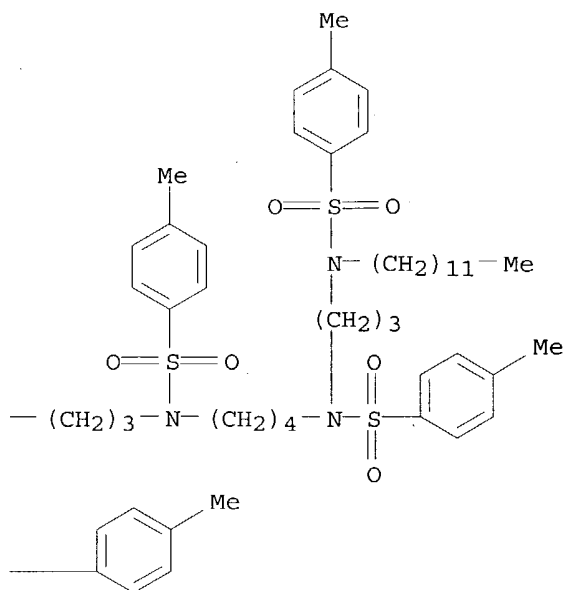


Cc1ccc(cc1)S(=O)(=O)N(CCC)N(CCCC)S(=O)(=O)c2ccc(C)cc2

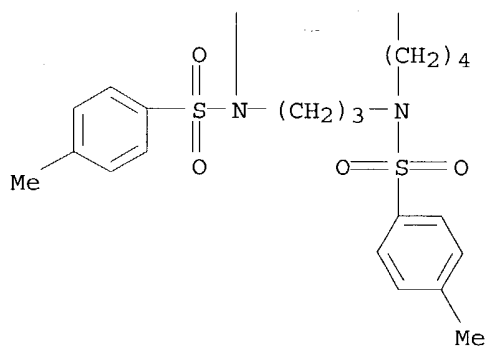
PAGE 1-A



PAGE 1-B

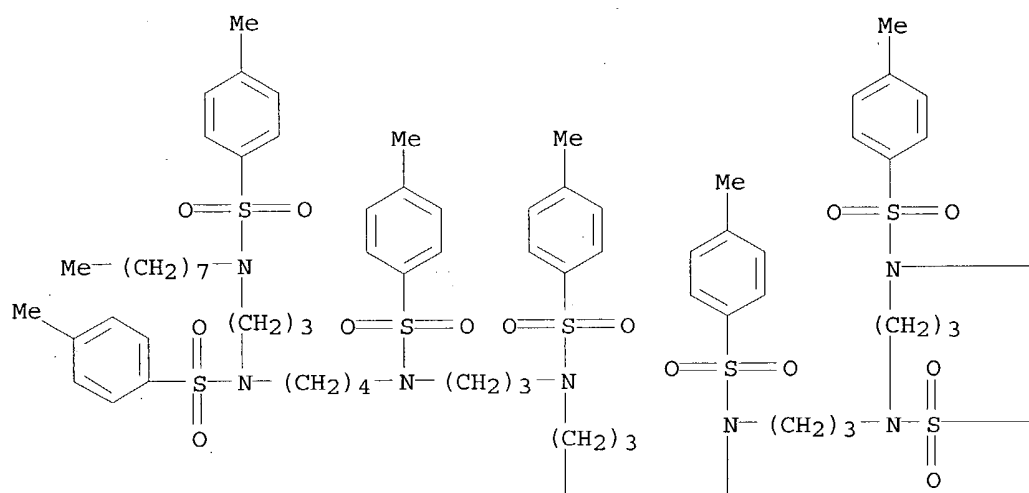


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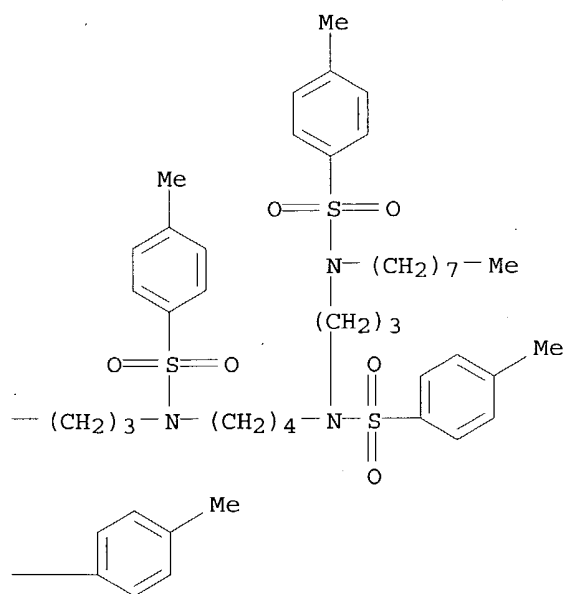


RN 239119-26-7 HCAPLUS  
 CN Benzenesulfonamide, N,N'-1,4-butanediylbis[4-methyl-N-[4,8,12,17,21-pentakis[(4-methylphenyl)sulfonyl]-4,8,12,17,21-pentaazanonacos-1-yl]-(9CI) (CA INDEX NAME)

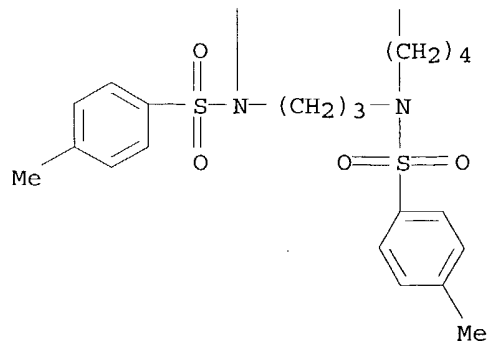
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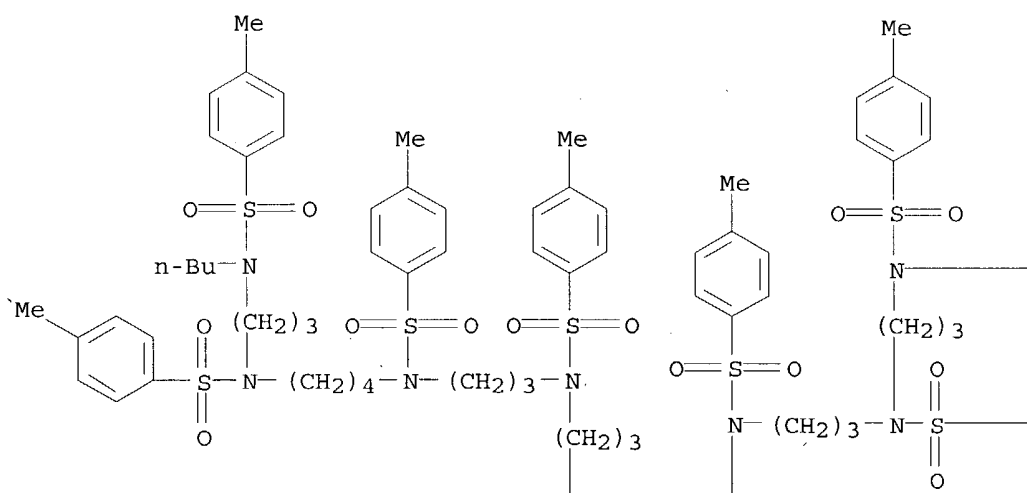


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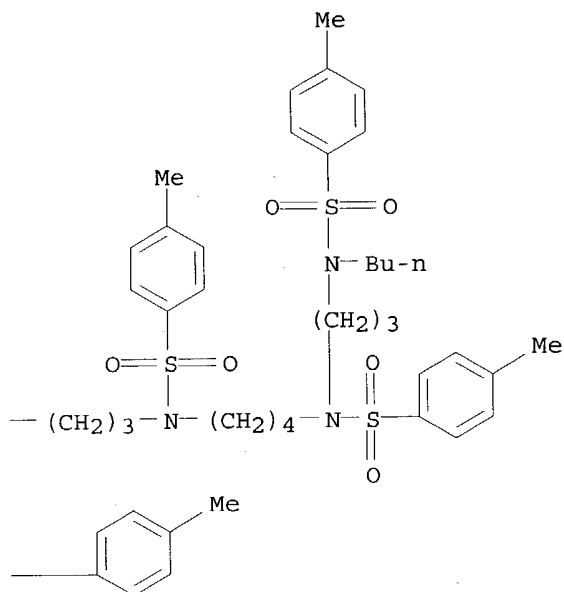
RN 239119-27-8 HCAPLUS  
 CN Benzenesulfonamide, N,N'-1,4-butanediylbis[4-methyl-N-[4,8,12,17,21-pentakis[(4-methylphenyl)sulfonyl]-4,8,12,17,21-pentaazapentacos-1-yl]-(9CI) (CA INDEX NAME)

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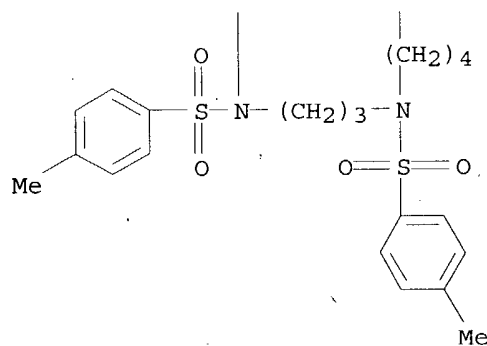




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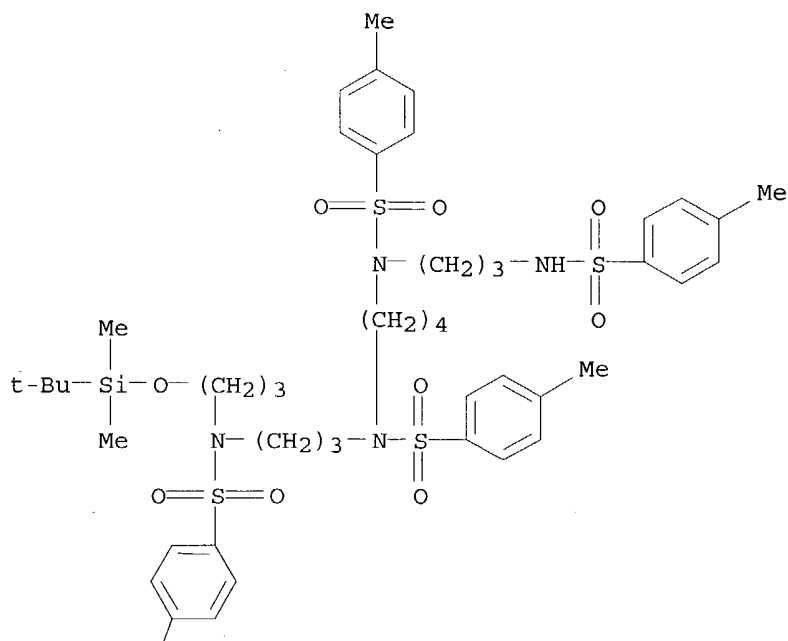


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RN 239119-32-5 HCAPLUS  
 CN Benzenesulfonamide, N-[3-[[3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]propyl  
 ][(4-methylphenyl)sulfonyl]amino]propyl]-4-methyl-N-[4-[[[(4-  
 methylphenyl)sulfonyl][3-[[[(4-methylphenyl)sulfonyl]amino]propyl]amino]but  
 yl]-(9CI) (CA INDEX NAME)

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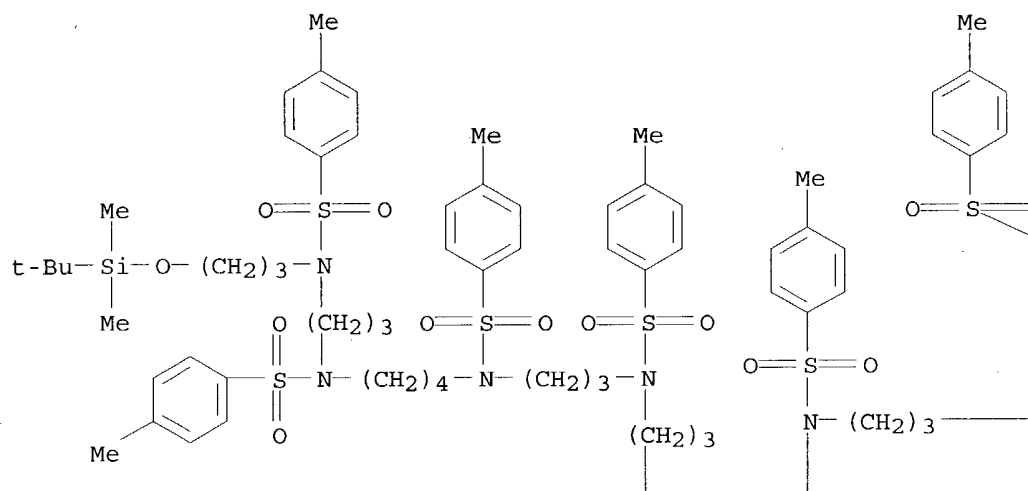


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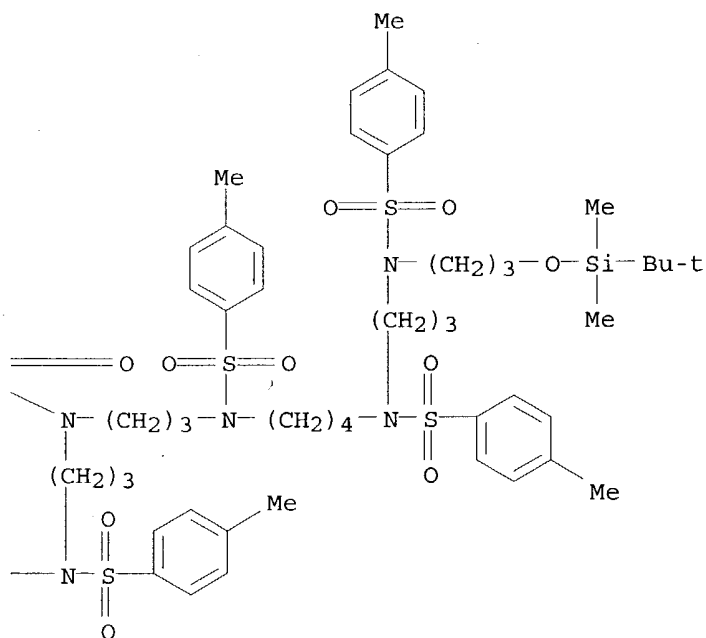


RN 239119-33-6 HCAPLUS  
 CN Benzenesulfonamide, N,N'-1,4-butanediylbis[4-methyl-N-[26,26,27,27-tetramethyl-4,8,12,17,21-pentakis[(4-methylphenyl)sulfonyl]-25-oxa-4,8,12,17,21-pentaaza-26-silaoctacos-1-yl]- (9CI) (CA INDEX NAME)

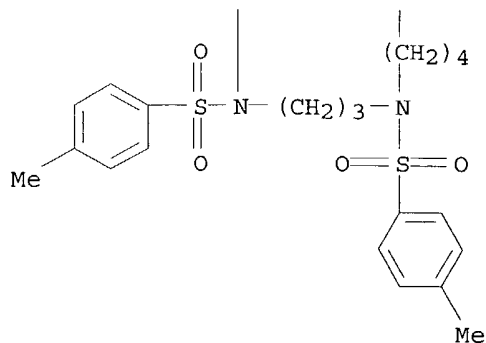
PAGE 1-A



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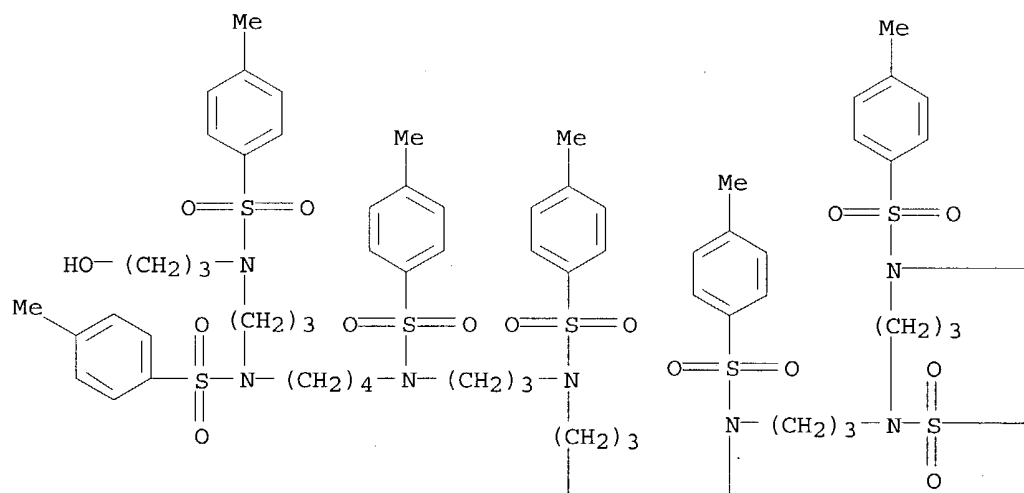


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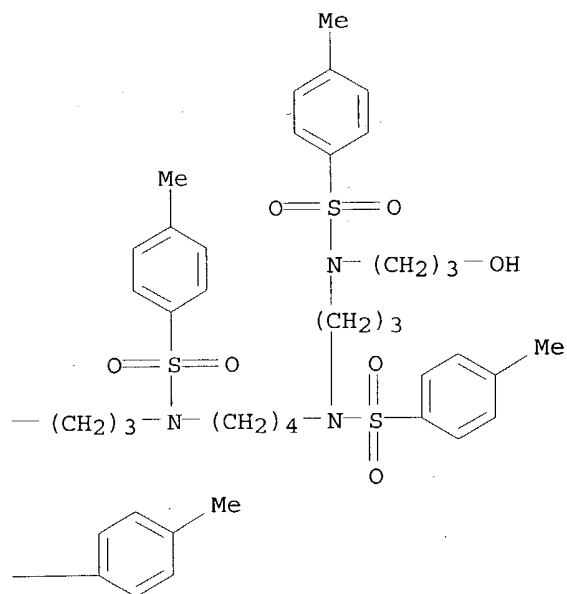


RN 239119-34-7 HCAPLUS  
 CN Benzenesulfonamide, N,N'-1,4-butanediylbis[N-[24-hydroxy-4,8,12,17,21-pentakis[(4-methylphenyl)sulfonyl]-4,8,12,17,21-pentaazatetracos-1-yl]-4-methyl- (9CI) (CA INDEX NAME)

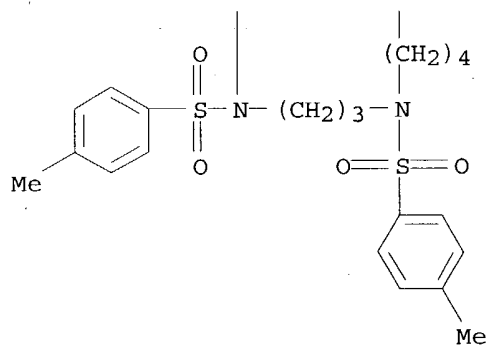
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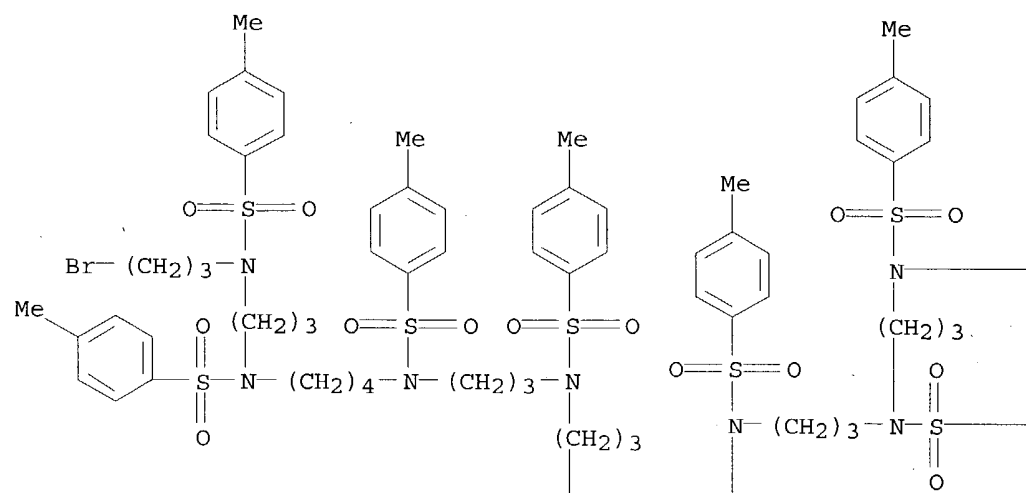


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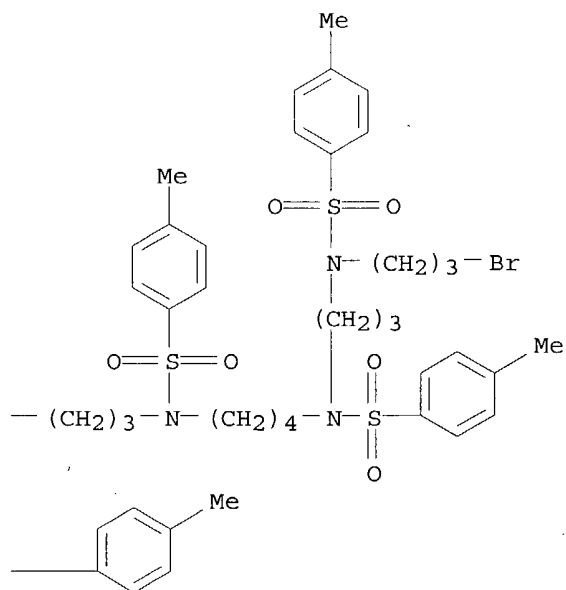


RN 239119-35-8 HCAPLUS  
 CN Benzenesulfonamide, N,N'-1,4-butanediylbis[N-[24-bromo-4,8,12,17,21-pentakis[(4-methylphenyl)sulfonyl]-4,8,12,17,21-pentaazatetracos-1-yl]-4-methyl- (9CI) (CA INDEX NAME)

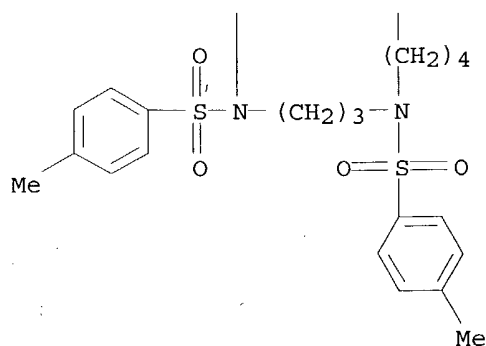
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RN 239480-83-2 HCAPLUS  
 CN Benzenesulfonamide, N,N'-1,4-butanediylbis[4-methyl-N-[4,8,12,17,21,25,29,34,38-nonakis[(4-methylphenyl)sulfonyl]-4,8,12,17,21,25,29,34,38-nonaazatetrapentacont-1-yl]- (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 112-29-8DP, Decyl bromide, reaction products with polyethyleneimine 112-71-0DP, Myristyl bromide, reaction products with polyethyleneimine 112-82-3DP, Cetyl bromide, reaction products with polyethyleneimine 112-89-0DP, Stearyl bromide, reaction products with polyethyleneimine 143-15-7DP, Lauryl bromide, reaction products with polyethyleneimine 9002-98-6DP, reaction products with alkyl bromides  
 239119-14-3P 239119-15-4P 239119-16-5P  
 239119-28-9P 239119-29-0P 239119-30-3P  
 239119-31-4P 239119-36-9P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of polyalkylimines as drug carriers)

RN 112-29-8 HCAPLUS  
 CN Decane, 1-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Me-(CH<sub>2</sub>)<sub>9</sub>-Br

RN 112-71-0 HCAPLUS  
 CN Tetradecane, 1-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Me-(CH<sub>2</sub>)<sub>13</sub>-Br

RN 112-82-3 HCAPLUS  
 CN Hexadecane, 1-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Me-(CH<sub>2</sub>)<sub>15</sub>-Br

RN 112-89-0 HCAPLUS  
 CN Octadecane, 1-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Me-(CH<sub>2</sub>)<sub>17</sub>-Br

RN 143-15-7 HCAPLUS  
CN Dodecane, 1-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

Me-(CH<sub>2</sub>)<sub>11</sub>-Br

RN 9002-98-6 HCAPLUS  
CN Aziridine, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 151-56-4  
CMF C2 H5 N



RN 239119-14-3 HCAPLUS  
CN 3,6,9,12,16,19,22,25,28,32,35,38,41-Tridecaazatritetracontane-1,43-diamine, N,N'-dihexadecyl- (9CI) (CA INDEX NAME)

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Me-(CH<sub>2</sub>)<sub>15</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-

PAGE 1-B

-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-

PAGE 1-C

-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-NH-CH<sub>2</sub>-CH<sub>2</sub>-

PAGE 1-D

-NH-(CH<sub>2</sub>)<sub>15</sub>-Me

RN 239119-15-4 HCAPLUS  
CN 3,6,9,12,16,19,22,25,28,32,35,38,41-Tridecaazatritetracontane-1,43-diamine, N,N'-didodecyl- (9CI) (CA INDEX NAME)



PAGE 1-A

 $\text{Me}-(\text{CH}_2)_{11}-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-$ 

PAGE 1-B

 $-\text{NH}-(\text{CH}_2)_3-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-$ 

PAGE 1-C

 $-\text{NH}-(\text{CH}_2)_3-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-$ 

PAGE 1-D

 $-\text{NH}-(\text{CH}_2)_{11}-\text{Me}$ 

RN 239119-16-5 HCAPLUS  
CN 3,6,9,12,16,19,22,25,28,32,35,38,41-Tridecaazatritetracontane-1,43-diamine, N,N'-dioctyl- (9CI) (CA INDEX NAME)

PAGE 1-A

 $\text{Me}-(\text{CH}_2)_7-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-$ 

PAGE 1-B

 $-\text{NH}-(\text{CH}_2)_3-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-$ 

PAGE 1-C

 $-\text{NH}-(\text{CH}_2)_3-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}_2-$ 

PAGE 1-D

 $-\text{NH}-(\text{CH}_2)_7-\text{Me}$ 

RN 239119-28-9 HCAPLUS  
CN 4,9,13,17,21,26,30,34,38,43-Decaazahexatetracontane-1,46-diamine, N,N'-dihexadecyl- (9CI) (CA INDEX NAME)

PAGE 1-A

 $\text{Me}-(\text{CH}_2)_{15}-\text{NH}-(\text{CH}_2)_3-\text{NH}-(\text{CH}_2)_4-\text{NH}-(\text{CH}_2)_3-\text{NH}-(\text{CH}_2)_3-\text{NH}-$

PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>4</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—

PAGE 1-C

— (CH<sub>2</sub>)<sub>4</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>15</sub>—Me

RN 239119-29-0 HCAPLUS

CN 4,9,13,17,21,26,30,34,38,43-Decaazahexatetracontane-1,46-diamine,  
N,N'-didodecyl- (9CI) (CA INDEX NAME)

PAGE 1-A

Me—(CH<sub>2</sub>)<sub>11</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>4</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—

PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>4</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—

PAGE 1-C

— (CH<sub>2</sub>)<sub>4</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>11</sub>—Me

RN 239119-30-3 HCAPLUS

CN 4,9,13,17,21,26,30,34,38,43-Decaazahexatetracontane-1,46-diamine,  
N,N'-dioctyl- (9CI) (CA INDEX NAME)

PAGE 1-A

Me—(CH<sub>2</sub>)<sub>7</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>4</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—

PAGE 1-B

— (CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>4</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—

PAGE 1-C

— (CH<sub>2</sub>)<sub>4</sub>—NH—(CH<sub>2</sub>)<sub>3</sub>—NH—(CH<sub>2</sub>)<sub>7</sub>—Me

RN 239119-31-4 HCAPLUS

CN 4,9,13,17,21,26,30,34,38,43-Decaazahexatetracontane-1,46-diamine,  
N,N'-dibutyl- (9CI) (CA INDEX NAME)

## PAGE 1-A

n-BuNH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>4</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-

## PAGE 1-B

-(CH<sub>2</sub>)<sub>4</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>4</sub>-NH-

## PAGE 1-C

-(CH<sub>2</sub>)<sub>3</sub>-NHBu-n

RN 239119-36-9 HCAPLUS

CN 4,9,13,17,21,26,30,34,38,43,47,51,55,60,64,68,72,77-Octadecaazaooctacontane-1,80-diamine, N,N'-dihexadecyl- (9CI) (CA INDEX NAME)

## PAGE 1-A

Me-(CH<sub>2</sub>)<sub>15</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>4</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-

## PAGE 1-B

-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>4</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-

## PAGE 1-C

-(CH<sub>2</sub>)<sub>4</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>4</sub>-NH-

## PAGE 1-D

-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-(CH<sub>2</sub>)<sub>4</sub>-NH-(CH<sub>2</sub>)<sub>3</sub>-NH-

## PAGE 1-E

-(CH<sub>2</sub>)<sub>15</sub>-Me

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